

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Simons *et al.*
Serial No. : 09/145,916
Filed : September 2, 1998
For : "STIMULATION OF ANGIOGENESIS VIA
ENHANCED ENDOTHELIAL EXPRESSION
OF SYNDECAN-4 PROTEINS"
Examiner : David Guzo
Group Art Unit : 1636
Attorney's Docket No . : BIS-039

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Assistant Commissioner for Patents, Washington, D.C. 20231
on: Feb. 6, 2002

Attorney for applicants:

David Trask

Signature:

David Trask

Date:

Feb. 6, 2002

MARKED UP VERSION OF AMENDED SPECIFICATION SUBMITTED
PURSUANT TO 37 C.F.R. 1.121(b)

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants, in fulfillment of and in accordance with the requirements
of 37 C.F.R. 121(b)(iii), hereby submit a marked up version of the instant

amendment to the Specification via marked-up replacement paragraphs,
this Specification amendment being directed to the paragraph at:

Page 29, line 23.

Respectfully submitted,

SIMONS *et al.*

By: 

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1 C. The Cytoplasmic Domain Coding For The Syndecan-4 Peptide

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3 The third requisite cytoplasmic domain must code for the amino acid
4 residue structure representative of the syndecan-4 core protein. As shown
5 experimentally by the data presented hereinafter, only the syndecan-4 cytoplasmic
6 region and peptide structure allows for functional stimulation of angiogenesis in-
7 situ. For this reason, it is essential and required in each embodiment of the
8 present invention that the third DNA sequence coding for the cytoplasmic domain
9 in the expressed proteoglycan entity in a transfected endothelial cell be
10 representative of and analytically identifiable as the syndecan-4 amino acid residue
11 structure. A representative recitation of the DNA constituting the cytoplasmic
12 domain of the syndecan-4 molecule is presented by Fig. 13 herein.

13 It will be noted and recognized that very little variability and substitution
14 within the specific DNA base sequencing of the cytoplasmic domain of the
15 syndecan-4 molecule is permitted. While some changes are expected, be they
16 point mutations, block substitutions and the like, the expected or envisioned degree
17 of variability which might be present or permitted for the cytoplasmic domain
18 DNA is believed to be quite limited.

19 As representative examples: The last four amino acids (EFYA) cannot be
20 changed or modified. Similarly, regarding the Serine residue at position 181: a
21 mutation to an Alanine residue potentiates activation; while a mutation to
22 Glutamate inhibits cell growth in a dominant fashion (dominant-negative mutation).
23 Finally, the LGKKPIYKK sequences [SEQ ID NO:24] probably cannot be altered at
24
25 all.